REMARKS

Claims 74-93 are under examination in this case. These claims stand rejected under 35 U.S.C. § 112, second paragraph and 35 U.S.C. § 102(b). In addition, claims 74, 75, 79-85, and 92 stand rejected under 35 U.S.C. § 112, first paragraph. Each of these issues is addressed below.

Amendments

Claims 74, 77, 80, 84, and 89 have been amended. These amendments find support, for example, in the specification as follows: claim 74, original claims 75 and 76, and page 5, line 16; claim 80, original claim 81; claim 84, page 10, line 27-page 11, line 13; and claim 89, page 11, lines 29-34. The amendment to claim 77 merely clarifies claim language. These amendments add no new matter.

Declaration

As requested, Applicants submit herewith a copy of the signed declaration for this application, originally submitted to the U.S. Patent Office on June 3, 2002.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 74-93 stand rejected under 35 U.S.C. § 112, second paragraph as being indefinite. The bases for this rejection are addressed below.

Claim 74 stands rejected because of the term "negligible reduction in the infectivity of the virus" and the assertion that it is unclear what degree of reduction is required. This term has been removed from claim 74, and the rejection is therefore moot. Claim 74 now simply requires that the virus including the modified structural protein maintain infectivity.

Claim 75 stands rejected as indefinite on the basis that it is unclear whether the claim is referring to viral particle formation or structural protein formation. Claim 75 is

canceled, but its language is incorporated into claim 74 in a way that now specifies that the claim refers to viral particle formation.

Claim 77 stands rejected based on the terms "derived from" and "derived therefrom." These terms have been deleted, and this basis for the rejection is therefore moot.

Claim 80 stands rejected based on the assertion that the term "high or low molecular weight compound(s)" is indefinite because this term is comparative and subject to individual interpretation. Claim 80 has been amended to remove this term and to specify particular compounds falling under the claim.

Claim 84 is asserted to also be indefinite because of the phrase "immunosuppressive protein or peptide." The Office asserts that the metes and bounds of this phrase cannot be determined. Applicants have amended claim 84 to recite particular proteins and peptides, and this basis for the rejection may be withdrawn.

And claim 89 stands rejected on the basis that the identity of the "XhoI/XhoI cleavage site" is unclear. This claim now specifies that it covers modifications of one or more deletions positioned between the XhoI/XhoI cleavage sites comprising 62 amino acids. This amendment is supported by the specification at page 11, lines 29-34, where it states "In a further preferred embodiment of the present invention, the modification(s) is(are) brought about by one or more deletions between the XhoI/XhoI cleavage sites of the VP1-encoding nucleic acid, which comprises 62 amino acids (Hermonat, P.L. et al. (1984), J. Virol., 51, 329-339)." From Applicants' amendment and the description in the specification, one skilled in the art would be apprised of the identity of the XhoI/XhoI fragment, and this final basis for the indefiniteness rejection may be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 74, 75, 79-85, and 92 stand further rejected, under 35 U.S.C. § 112, first paragraph as lacking enablement. As applied to the current claims, this rejection is

respectfully traversed.

The Office states that "the specification, while being enabling for a method for reducing the antigenicity of adeno-associated virus (AAV) comprising modifying the capsid (VP), does not reasonably provide enablement for reducing antigenicity of AAV comprising the modification of any structural protein."

As the current claims are limited to methods for reducing antigenicity that require modification of a "structural protein of AAV, the structural protein being selected from the group consisting of AAV VP1, VP2, and VP3," they cover only subject matter acknowledged by the Office to be enabled. This rejection may be withdrawn.

Rejection under 35 U.S.C. § 102(b)

Claims 74-93 stand further rejected under 35 U.S.C. § 102(b) as being anticipated by Mamounas *et al.* (WO 97/38723). As applied to the present claims, this rejection is respectfully traversed.

The present claims are directed to a method for reducing the antigenicity of AAV by introducing at least one modification into an AAV structural protein, VP1, VP2, or VP3. The claims further require that the modified structural protein form AAV particles and that the AAV having the modified structural protein retain infectivity. Nowhere is this claimed invention disclosed by Mamounas.

As indicated previously, Mamounas does not disclose a mutated AAV structural protein that is capable of supporting viral particle formation, as required by claim 74 and its dependent claims. Indeed, the only construct tested by Mamounas, as indicated at page 68, lines 13-14, "failed to produce any intact viral particles." In particular, Mamounas states (page 68, ll. 14-18; emphasis added):

> To overcome this obstacle [the failure to produce any intact viral particles], we included *wild type AAV capsid proteins* into the packaging process. We employed a triple plasmid DNA co-transfection strategy, namely co-infecting cells with (1) *pAV/Ad [a rAAV vector encoding wild-type capsid protein; page 64, line 31]*, (2)

> pAAVgal conjugated to polylysine coupled adenovirus, and (3) the individual pVP-scFv chimeric protein-containing plasmid.

Thus, the only way that Mamounas could produce intact viral particles using this construct was to include in their transfection system a helper vector encoding wild-type capsid protein. That wild-type capsid protein was necessary for viral particle formation. The Mamounas modified capsid protein was not capable of forming AAV particles, and the Mamounas virus was not infective on its own.

In response to this position, the Office, in the latest Action, states that:

> Applicant is arguing about limitations that are not in the claims. Specifically, the claims are not limited to a method that results in an intact viral particle that is accomplished only by the recited steps of introducing a modification. Since the method using the term, "comprising", the method is open-ended and includes any number of additional steps. Mamounas' method does what Applicant's method does, with the additional steps of a triple-plasmid strategy in order to get an intact particle. Mamounas' method results in the same product, but with additional steps. The open claim language does not preclude the steps taken by Mamounas.

As applied to the current claim language, this rejection should be withdrawn. The present claims require that the "*modified* structural protein *forms AAV particles* and the AAV *having* the *modified* structural protein *retains infectivity*." These claim requirements specify that it is the *modified capsid protein* (not a second or third plasmid construct) that must be capable of forming the viral particles and that it is the AAV *having* that modified capsid that retains infectivity. Neither of these requirements is met by the Mamounas triple-plasmid system. The § 102(b) rejection may be withdrawn.

CONCLUSION

Applicant submits that the claims are in condition for allowance, and such action is respectfully requested.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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